REMARKS

Claims 1-11 are all the claims pending in the application. Of these claims, claims 4-6 are withdrawn from further consideration as being drawn to a nonelected invention. Claim 3 is withdrawn as being drawn to a non-elected species, there being no allowable generic or linking claim, but should be added back if claim 1 is found allowable. Claims 1, 2, and 7-11 are rejected.

I. Amendments to the Claims

Claim 1 has been amended to recite a method for inhibiting CCR3, comprising administering a CCR3-antagonistic compound of formula (I). Support for this amendment can be found throughout the specification, especially at Examples 1 and 2, pages 250-253 of the specification.

Claim 7 has been amended to recite a method for treatment and/or prevention of various specific CCR3-related diseases, comprising administering a CCR3-antagonistic compound of formula (I). Support for this amendment can be found at pages 1-4 of the specification.

Claims 1 and 7 have also been amended to recite that when k is 1 and m is 2, then n is not 1.

Claim 2 has been amended to recite the methods of claim 1, and claims 8-11 have been amended to recite the methods of claim 7.

Finally, several minor amendments have been made to clarify the language of claim 1. These amendments are editorial in nature and are not intended to limit the scope of the claims.

II. Information Disclosure Statement

The Examiner has not yet returned an initialed copy of the PTO Form 1449 which accompanied the Information Disclosure Statement filed on April 23, 2002. Applicants have included a copy of the PTO Form 1449 (which accompanied the IDS filed April 23, 2002), and again respectfully request the Examiner to initial it thereby indicating that all references have been considered.

III. Detailed Action

A. Claim Objection – Informalities

At page 2 of the Office Action, claim 1 was objected to because of the following informalities: the employment of a bracket "[ ]," and the employment of parenthetical expressions.

Applicants have amended claim 1 to remove the brackets and the parenthetical expressions. Several additional minor grammatical informalities have also been corrected. Accordingly, Applicants respectfully request reconsideration and withdrawal of the objection.

B. Claim Rejections – Double Patenting

At pages 2-3, paragraphs 3-4 of the Office Action, claims 1, 2, and 7-11 were rejected under the judicially created doctrine of obviousness-type double patenting, as being unpatentable over claims 1-11, 27-37 of Shiota et al., U.S. Patent No. 6,451,842. At page 3, paragraph 4, the Examiner states that although the conflicting claims are not identical, they are not patentably distinct, because Shiota claims compounds that encompass and substantially overlap Applicant's elected species.

An obviousness-type double patenting rejection does not apply where the patent principally underlying the rejection is prior art. See, e.g., *General Foods Corp. v. Studiengesellschaft*, 972 F.2d 1272, 1281, (Fed. Cir. 1992). Thus, because Shiota qualifies as prior art under 35 U.S.C. § 102(e), the rejection is improper and should be removed.

C. Claim Rejections Under 35 U.S.C. § 112 - Enablement

At pages 3-5, claims 1, 2, and 7-11 were rejected for failing to meet the enablement requirement of 35 U.S.C. § 112, first paragraph.

At page 3, paragraph 6 of the Office Action, the Examiner acknowledged that because the specification discloses that the claimed compositions are CCR3 antagonists, and may be useful in alleviating or suppressing the symptoms of the specified diseases, the specification is enabling for *treating* the diseases enumerated in claims 8-11. However, the Examiner stated that because each of the listed diseases may have different etiologies, the specification and the claims do not

provide sufficient evidence or working examples showing that the CCR3 antagonists would be useful for *preventing* such diseases. See page 4, paragraph 1.

In addition, at page 4, paragraph 2, the Examiner pointed out that claim 7 defines diseases treatable by the composition herein as "diseases concerned with CCR3," and asserts that the specification fails to either identify what other diseases besides those listed in claims 8-11 are "CCR3 concerned" diseases, or provide information allowing the skilled artisan to ascertain such diseases without undue experimentation.

As noted above, claim 1 has been amended to recite a method for inhibiting CCR3, comprising administering a CCR3-antagonistic compound of formula (I). Claim 7 has been amended to recite a method for treatment or prevention of various specified diseases involving the CCR3 receptor. Applicants submit that the claims are fully enabled by the specification, for at least the following reasons.

1. Claim 1. With regard to claim 1, Applicants have clearly shown that the compounds of the present invention act as CCR3 inhibitors to inhibit CCR3 activity. The results presented in Example 1, for instance, demonstrate that the compounds inhibit the eotaxin-mediated rise in intracellular calcium levels in cells expressing CCR3 receptor (see pages 250-252 of the present specification). The results of Example 2 show that the compounds act to inhibit eotaxin binding to target CCR3-expressing cells (pages 252-253). Furthermore, methods of administering small molecular weight compounds such as the compounds of the present invention are described at pages 18 and 19 of the present specification, and are well known in the art.

2. Claim 7. As noted above, the Examiner indicated in the outstanding Office Action that the specification is enabling for use of the recited compounds to treat the various CCR3-related diseases listed in claims 8-11. Claim 7 recites several additional CCR3-related diseases that are not specifically listed in claims 8-11. The additional diseases are disclosed at page 1, lines 10-16 of the specification, and involvement of the diseases with the CCR3 receptor is detailed at pages 1-4. Applicants submit that use of the compounds to treat the additional CCR3-related diseases is enabled for the same reasons put forth by the Examiner regarding the diseases listed in claims 8-11 (see above).

The Examiner also indicated that although the specification enables treatment of diseases involving CCR3, it does not enable prevention of these diseases. Applicants respectfully disagree, and submit that the specification does enable prevention as well as treatment of CCR3-related diseases, for at least the following reasons.

Because the underlying mechanisms involved in prevention and treatment of disease are often the same, the same medication can frequently be used for both purposes. For example, a preventative medicine can suppress development of a disease to the first disease stage; similarly, a medicine used for treatment can prevent progression of the disease to a more advanced stage. In other words, both prevention and treatment involve targeting disease stages, and the mechanisms by which medication suppresses disease can be essentially identical in the case of prevention and treatment. Please see, for example, the attached reference, which describes a distamycin analogue that inhibits chemokine binding to chemokine receptors and acts to block

chemokine-induced calcium flux, and is considered an attractive candidate for treatment as well as prevention of AIDs. Howard et al., J. Med. Chem. 1998, 41, 2184-2193.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the enablement rejection.

D. Claim Rejections Under 35 U.S.C. § 112 – Indefiniteness

At pages 5-6, paragraphs 8-9 of the Office Action, claims 1, 2, and 7-11 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

The Examiner stated that the phrase "arbitrary number of halogen atoms" in claim 1 has not been clearly defined in either the claim or the specification. Thus, the claims are indefinite as to the number of halogen atoms therein.

Applicants have amended claim 1 by substituting the phrase "one or more halogen atoms" for the phrase "arbitrary number of halogen atoms," wherever it appears in the claims. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

Applicants also wish to point out for the record that the qualifying phrase "can be substituted by one or more" in claim 1 refers not only to halogen atoms, but also to various other potential substituents subsequently listed.

D. Claim Rejections Under 35 U.S.C. § 103(a) – Obviousness

1. Shiota et al. At pages 6-7, paragraphs 12-15 of the Office Action, claims 1, 2, and 7-11 were rejected under 35 U.S.C. § 103(a), as being unpatentable over Shiota et al., U.S. Patent No. 6,451,842 and WO 99/25686.

The Examiner explained that Shiota discloses therapeutic compounds with a general formula essentially identical to Applicants's formula (I). Although Shiota does not expressly teach the particular species elected by Applicants, the general formula taught by Shiota encompasses the species. The Examiner cites Examples 243-247 of Shiota as being structurally close to the elected species. Thus, the Examiner concludes that the compounds claimed in the instant invention would be obvious to a person of ordinary skill in the art at the time the invention was made.

As noted above, Applicants have amended the claims to recite methods of using the compounds to inhibit CCR3 activity (claims 1 and 2) and treat diseases involving CCR3 (claims 7-11).

Applicants respectfully submit that the claims of the present invention are not obvious in light of Shiota. The reference does not teach or suggest inhibition of CCR3 activity or even interaction of compounds with CCR3 receptors. Furthermore, the reference does not teach or suggest use of compounds for treating allergic diseases or any of the other CCR3-related diseases specified in claims 7-11.

The target diseases disclosed by Shiota all involve the binding of chemokines to particular chemokine receptors on the cell surface. Specifically, the chemokine receptors

described by Shiota are CCR1, CCR2A, and CCR2B, which interact with chemokines MIP-1α and/or MCP-1. The chemokines described in the reference are not ligands of CCR3. In addition, the receptors described in the reference do not interact with the CCR3 ligand eotaxin.

Accordingly, one of ordinary skill in the art at the time of the instant invention would not have reasonably expected the compounds of Shiota to be useful for inhibiting CCR3 or for treating CCR3-related diseases. Thus, use of the compounds recited in the present claims for inhibiting CCR3, and for treating and preventing diseases involving CCR3 receptors, is not obvious in light of Shiota.

In view of the above, Applicants respectfully request reconsideration and withdrawal of the rejection.

2. Rogers et al. At page 7, paragraphs 16-18, claims 1, 2, and 7-11 were rejected under 35 U.S.C. § 103(a), as being unpatentable over Rogers et al., U.S. Patent No. 6,166,015 (hereinafter "Rogers").

At page 7, paragraphs 17 and 18 of the Office Action, the Examiner explained that Rogers teaches pyrolidine-derivative CCR3 receptor antagonists useful for treating CCR3-associated diseases, such as asthma. In addition, the Examiner stated that the general formula (I) in Rogers substantially overlaps with the general formula (I) claimed by Applicants. The Examiner concluded that while Rogers does not expressly teach a pharmaceutical composition comprising the compounds claimed by Applicants, such composition would be obvious to a person of ordinary skill in the art in light of Rogers.

Claims 1 and 7 have been amended to recite that when k is 1 and m is 2, then n is not 1. As a result, the compounds recited in the instant claims are not encompassed by the compounds of general formula (I) in Rogers. Furthermore, the general formula disclosed by Rogers does not encompass compound 2296, the particular species elected by Applicants in the Response to Restriction and Election of Species filed July 25, 2003. Specifically, compound 2296 differs from the general formula (I) disclosed in Rogers at least in that the methylene group between A and the 5-membered ring containing Z in Rogers is not present in the elected species.

Because Rogers does not teach or suggest the structure of the compounds recited in the present claims, one of skill in the art would not have reasonably expected the compounds to have CCR3 receptor antagonist activity. Therefore, use of the compounds to inhibit CCR3 receptor, and to treat and prevent diseases involving CCR3 receptor, is not obvious in light of Rogers.

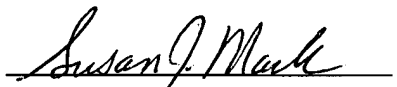
Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

IV. Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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